IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Clark et al. Application No: 10/627,591 Confirmation No: 2973 Filed: July 25, 2003 Title: AEROSOLIZED ACTIVE AGENT DELIVERY	Group Art Unit: 3771 Examiner: Douglas, Steven O Attorney Docket No: 53229-US-CNT[2] (NK.0029.10) May 13, 2009 San Francisco, California

APPEAL BRIEF

VIA ELECTRONIC FILING

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Examiner:

In response to the Examiner's Final Rejection of December 19, 2008 and the Advisory Action of March 6, 2009, the Applicant of the above-referenced patent application (hereinafter Appellant) hereby appeals to the Board of Patent Appeals and Interferences. Appellant requests the reversal of the Final Rejection.

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By: Melanie Hitchcock
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Date: May 13, 2009

(1) *Real Party in Interest*

The real party in interest of the present application is Novartis AG (by way of assignment from Novartis Pharmaceuticals AG and from Nektar Therapeutics, which was formerly Inhale Therapeutic Systems, Inc.), having a place of business at Forum 1, Novartis Campus, CH-4056 Basel, Switzerland.

(2) *Related Appeals and Interferences*

Appellant, Appellant's legal representative, and assignee are aware of no appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

(3) *Status of Claims*

Claims 23-52 are presently pending in the case. Claims 1-22 have been cancelled. Claims 25 and 27 have been withdrawn from consideration until such time as they depend from an indicated allowable generic claim. Claims 23, 24, 26 and 28-52 have been finally rejected. The rejection of each of claims 23, 24, 26 and 28-52 is hereby appealed.

(4) *Status of Amendments*

An After Final amendment was filed on February 19, 2009. In an Advisory Action of March 6, 2009, the Examiner indicated that the After Final Amendment would be entered for the purposes of appeal. Accordingly, all amendments made during prosecution of the case have been entered.

(5) *Summary of the Claimed Subject Matter*

As recited in claim 23, a device (see reference numerals 100, 200 and 300 in Figures 1-3) increases the bioavailability of an aerosolized active agent (see page 8 lines 24-32). The device (100, 200, 300) comprises a flow restrictor (see reference numeral 102 in Figures 1A and 1B, reference numeral 212 in Figures 2A and 2B, reference numeral 302 in Figures 3A and 3B and the arrangements shown in Figures 4A, 5A, 6A and 7A) for limiting the inspiratory flow of an aerosolized active agent formulation to a human patient to less than 17 liters per minute (page 8 lines 24-32), wherein the device is adapted to aerosolize the active agent formulation and wherein the active agent formulation is (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant (see page 9 lines 1-16).

As recited in claim 33, a device (see reference numerals 100, 200 and 300 in Figures 1-3) delivers an aerosolized active agent to the lungs of a human patient. The device (100, 200, 300) is adapted to deliver an aerosolized active agent formulation at an inspiratory flow rate limited to a rate less than 17 liters per minute (see reference numeral 102 in Figures 1A and 1B, reference numeral 212 in Figures 2A and 2B, reference numeral 302 in Figures 3A and 3B and the arrangements shown in Figures 4A, 5A, 6A and 7A and see page 8 lines 24-32)), wherein the device is adapted to aerosolize the active agent formulation and wherein the active agent formulation is (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant (see page 9 lines 1-16).

As recited in claim 38, a device (see reference numerals 100, 200 and 300 in Figures 1-3) delivers aerosolized insulin to the lungs of a human patient (see page 14 lines 25-32), wherein said device (100, 200, 300) comprises a flow restrictor (see reference numeral 102 in Figures 1A and 1B, reference numeral 212 in Figures 2A and 2B, reference numeral 302 in Figures 3A and 3B and the arrangements shown in Figures 4A, 5A, 6A and 7A) to restrict an inspiratory flow rate of an aerosolized insulin formulation to less than 17 liters per minute (see page 8 lines 24-32) and wherein the

device is adapted to aerosolize the insulin (see page 9 lines 1-16).

As recited in claim 42, a device (see reference numerals 100, 200 and 300 in Figures 1-3) delivers an aerosolized active agent to the lungs of a human patient. The device (100, 200, 300) comprises one or more orifices (see reference numerals 102 and 103 in Figures 1A and 1B, reference numerals 212 and 214 in Figures 2A and 2B, reference numerals 302 and 318 in Figures 3A and 3B and the arrangements shown in Figures 4A, 5A, 6A and 7A) sized so that an aerosolized active agent formulation may be delivered at an inspiratory flow rate that is limited to a rate of less than 17 liters per minute (see page 8 lines 24-32), wherein the device is adapted to aerosolize the active agent formulation and wherein the active agent formulation is (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant (see page 9 lines 1-16).

As recited in claim 47, a device (see reference numerals 100, 200 and 300 in Figures 1-3) delivers an aerosolized active agent to the lungs of a human patient. The device (100, 200, 300) comprises a chamber (112, 200, 306) in flow communication with a mouthpiece (114, 304); means for aerosolizing the active agent (page 9 lines 1-16); and means for limiting an inspiratory flow rate through the mouthpiece to less than 17 liters per minute (see reference numeral 102 in Figures 1A and 1B, reference numeral 212 in Figures 2A and 2B, reference numeral 302 in Figures 3A and 3B and the arrangements shown in Figures 4A, 5A, 6A and 7A and page 8 lines 24-32), whereby an aerosolized active agent formulation in the chamber may be delivered to the human patient, the active agent formulation being (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant (page 9 lines 1-16).

(6) *Grounds of Rejection to be Reviewed on Appeal*

Appellant requests review of the Examiner's following grounds of rejection:

Claims 23, 24, 26 and 28-52 have been rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent 5,735,263 to Rubsamen et al (hereinafter Rubsamen et al).

(7) *Argument*

Appellant believes each of claims 23, 24, 26 and 28-52 is improperly rejected and is therefore allowable for the following reasons.

The rejection of independent claim 23 under 35 U.S.C. §102(e) is improper

Rubsamen et al does not anticipate independent claim 23. For a rejection under 35 USC §102 to be proper, the reference relied upon must disclose each and every element of the claimed invention. Non-disclosure of a single element, feature or limitation of the claim negates anticipation. Claim 23 positively sets forth elements that are not disclosed by Rubsamen et al.

Claim 23 is to a device for increasing the bioavailability of an aerosolized active agent. The device comprises, inter alia, a flow restrictor for limiting the inspiratory flow of an aerosolized active agent formulation to a human patient to less than 17 liters per minute. This positively recited feature is not disclosed by Rubsamen et al. Rubsamen et al discloses no flow restrictor for limiting the inspiratory flow of an aerosolized active agent. Furthermore, Rubsamen et al does not in any way limit the inspiratory flow to less than 17 liters per minute. Instead, Rubsamen et al discloses an inhalation device where the inspiratory flow rate is not limited as claimed by Appellant. For example, as can be seen in Figures 5-9 and in column 5 lines 50-55 of Rubsamen et al, flow rates

much higher than 17 liters per minute can easily be achieved by a patient using the device under normal conditions. Since Rubsamen et al does not disclose each and every feature set forth in claim 23, it does not anticipate the claim.

Rubsamen et al is not a flow limiting device and the characterization of it as such is in error. Rubsamen et al ***measures*** inspiratory flow rate, but does not ***limit*** inspiratory flow rate. See column 6 lines 45-52 and column 12 lines 14-27. Rubsamen et al releases a dose of drug at a particular measured inspiratory flow rate. That Rubsamen et al discloses delivering drug at inspiratory flow rates below 17 liters per minute has no relevance to whether or not Rubsamen et al limits the flow rate as claimed by Appellant. Regardless of the inspiratory flow rate at which the drug is delivered, Rubsamen et al does not limit the flow rate as claimed by Appellant. In other words, a user of the Rubsamen et al device may have drug start to be administered at flow rates below 17 liters per minute and then may inspire at flow rates significantly above 17 liters per minutes while the drug continues to be administered.

The Examiner's comments in the Final Rejection of December 19, 2008 do not serve to establish Rubsamen et al as an anticipatory reference. For example, the Examiner refers to recitations within Rubsamen et al, such as column 5 lines 50-55, that are purported to support the Examiner's position that Rubsamen et al teaches limiting the flow rate. However, the recitations do not in actuality teach that which the Examiner contends. In the recitation in column 5, Rubsamen et al is merely referring to the flow rates at which the aerosolized formulation may be released into the inhalation stream. Thus, Rubsamen et al does not disclose or teach all that is claimed by Applicant in claim 23.

In another attempt to show anticipation, the Examiner refers to a solenoid valve (9) in Rubsamen et al. However, Rubsamen et al does not disclose that the solenoid valve (9) limits the flow rate as recited in Applicant's claim 23. The valve (9) in Rubsamen et al instead is opened to allow a formulation to be aerosolized when a patient's inhalation flow rate is measured to have reached a predetermined amount (see

column 24 line 22 though column 25 line 33). Rubsamen et al does not disclose a restrictor that restricts flow. Using the Rubsamen et al device, a patient may inhale at flow rates significantly higher than 17 liters per minutes. The valve (9) of Rubsamen et al also fails to meet the limitations of claim 23 when it is in its closed position where it prevents release of the drug. First, in the valve's closed position there is no flow of aerosolized active agent. Accordingly, there is no flow to limit. Secondly, claim 23 is directed to limiting inspiratory flow. Even when valve (9) is closed, there is no limitation on the user's inspiratory flow, *i.e.,* the user may inspire as freely as when the valve (9) is open. Thus, the Examiner's comments with regard to the valve (9) of Rubsamen et al are of no moment.

In the Advisory Action, the Examiner states that Rubsamen et al "is certainly capable of achieving flow rates less than 17 liters per minute if desired." However, this statement does not show anticipation of Appellant's claim 23. The invention of claim 23 is not directed merely to the administration of active agent at flow rates below 17 liters per minute, it is directed to ***limiting*** the administration to flow rates below 17 liters per minute. While the Examiner's statement may or may not be true, the Rubsamen et al device certainly is ***not*** capable of ***limiting*** flow rates to less than 17 liters per minute. Absent this positively recited feature, Rubsamen et al does not anticipate claim 23.

Applicant requests reversal of the rejection of claim 23 under 35 U.S.C. §102(e). In addition, Applicant requests reversal of the rejection of claims 24, 26 and 28-32 which depend from claim 23 and are not anticipated by Rubsamen et al for at least the same reasons as claim 23.

<u>The rejection of independent claim 33 under 35 U.S.C. §102(e) is improper</u>

Independent claim 33 is also not anticipated by Rubsamen et al. Claim 33 is to a device for delivering an aerosolized active agent to the lungs of a human patient, wherein said device is adapted to deliver an aerosolized active agent formulation at an inspiratory flow rate limited to a rate less than 17 liters per minute. Rubsamen et al

does not disclose a device that limits inspiratory flow rate to a rate less than 17 liters per minute. Therefore, Rubsamen et al does not anticipate claim 33.

Applicant requests reversal of the rejection of claim 33 under 35 U.S.C. §102(e). In addition, Applicant requests reversal of the rejection of claims 34-37 which depend from claim 33 and are not anticipated by Rubsamen et al for at least the same reasons as claim 33.

The rejection of independent claim 38 under 35 U.S.C. §102(e) is improper

Rubsamen et al does not anticipate independent claim 38, either. Claim 38 is to a device comprising, inter alia, a flow restrictor to restrict an inspiratory flow rate of an aerosolized formulation to less than 17 liters per minute. Rubsamen et al does not anticipate claim 38 in that it does not disclose a flow restrictor to restrict an inspiratory flow rate of an aerosolized formulation to less than 17 liters per minute.

Applicant requests reversal of the rejection of claim 38 under 35 U.S.C. §102(e). In addition, Applicant requests reversal of the rejection of claims 39-41 which depend from claim 38 and are not anticipated by Rubsamen et al for at least the same reasons as claim 38.

The rejection of independent claim 42 under 35 U.S.C. §102(e) is improper

Independent claim 42 is also not anticipated by Rubsamen et al. Claim 42 is to a device for delivering an aerosolized active agent to the lungs of a human patient, wherein said device comprises one or more orifices sized so that an aerosolized active agent formulation may be delivered at an inspiratory flow rate that is limited to a rate of less than 17 liters per minute. Rubsamen et al does not disclose orifices sized so that an aerosolized active agent formulation may be delivered at an inspiratory flow rate of less than 17 liters per minute. Thus, Rubsamen et al does not anticipate claim 42.

Applicant requests reversal of the rejection of claim 42 under 35 U.S.C. §102(e). In addition, Applicant requests reversal of the rejection of claims 43-46 which depend from claim 42 and are not anticipated by Rubsamen et al for at least the same reasons as claim 42.

The rejection of independent claim 47 under 35 U.S.C. §102(e) is improper

Independent claim 47 is also not anticipated by Rubsamen et al. Claim 47 is to a device for delivering an aerosolized active agent to the lungs of a human patient, said device comprising, inter alia, means for limiting an inspiratory flow rate to less than 17 liters per minute. Rubsamen et al does not disclose a means for limiting an inspiratory flow rate to less than 17 liters per minute. Accordingly, Rubsamen et al does not anticipate claim 47.

Applicant requests reversal of the rejection of claim 47 under 35 U.S.C. §102(e). In addition, Applicant requests reversal of the rejection of claims 48-52 which depend from claim 47 and are not anticipated by Rubsamen et al for at least the same reasons as claim 47.

Conclusion

Thus, it is believed that all rejections made by the Examiner have been addressed and overcome by the above arguments. Therefore, all pending claims are allowable. A reversal is respectfully requested.

Should there be any questions, Appellant's representative may be reached at the number listed below.

Respectfully submitted,

JANAH & ASSOCIATES

Dated: May 13, 2009

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(8) Claims Appendix

23. A device for increasing the bioavailability of an aerosolized active agent, said device comprising a flow restrictor for limiting the inspiratory flow of an aerosolized active agent formulation to a human patient to less than 17 liters per minute, wherein the device is adapted to aerosolize the active agent formulation and wherein the active agent formulation is (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant.

24. The device of claim 23 wherein the flow restrictor comprises an orifice.

25. The device of claim 24 wherein the flow restrictor comprises apertures of 0.5 to 0.9 mm in diameter.

26. The device of claim 23 wherein the flow restrictor is a valve that provides for decreasing resistance with increasing flow rate.

27. The device of claim 23 wherein the flow restrictor is a valve that provides for high resistance at all flow rates except a desired flow rate range.

28. The device of claim 23 wherein the device is adapted to be used with an active agent selected from the group consisting of insulin, cyclosporin, parathyroid hormone, follicle stimulating hormone, alpha-1-antitrypsin, budesonide, human growth hormone, growth hormone releasing hormone, interferon alpha, interferon beta, growth colony stimulating factor, leutinizing hormone releasing hormone, calcitonin, low molecular weight heparin, somatostatin, respiratory syncytial virus antibody, erythropoietin, Factor VIII, Factor IX, ceredase, cerezyme and analogues, agonists and antagonists thereof.

29. The device of claim 23 wherein the active agent formulation is a powder and wherein the device is adapted to aerosolize the active agent formulation.

30. The device of claim 23 wherein the active agent formulation is contained in a blister and wherein the device is adapted to receive the blister.

31. The device of claim 23 wherein the device is adapted to aerosolize a powder active agent formulation.

32. The device of claim 31 wherein the device is adapted to aerosolize the powder active agent formulation using compressed air.

33. A device for delivering an aerosolized active agent to the lungs of a human patient, wherein said device is adapted to deliver an aerosolized active agent formulation at an inspiratory flow rate limited to a rate less than 17 liters per minute, wherein the device is adapted to aerosolize the active agent formulation and wherein the active agent formulation is (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant.

34. The device of claim 33 wherein the device is adapted to be used with an aerosolized active agent formulation in dry powder form.

35. The device of claim 33 wherein the device is adapted to deliver the aerosolized active agent formulation at an inspiratory flow rate limited to a rate of 10 liters per minute or less.

36. The device of claim 33 wherein the active agent formulation is a powder and wherein the device is adapted to aerosolize the active agent formulation.

37. The device of claim 33 wherein the active agent formulation is contained in a blister and wherein the device is adapted to receive the blister.

38. A device for delivering aerosolized insulin to the lungs of a human patient, wherein said device comprises a flow restrictor to restrict an inspiratory flow rate of an aerosolized insulin formulation to less than 17 liters per minute and wherein the device is adapted to aerosolize the insulin.

39. The device of claim 38 wherein the inspiratory flow rate is 10 liters per minute or less.

40. The device of claim 38 wherein the active agent formulation is a powder and wherein the device is adapted to aerosolize the active agent formulation.

41. The device of claim 38 wherein the active agent formulation is contained in a blister and wherein the device is adapted to receive the blister.

42. A device for delivering an aerosolized active agent to the lungs of a human patient, wherein said device comprises one or more orifices sized so that an aerosolized active agent formulation may be delivered at an inspiratory flow rate that is limited to a rate of less than 17 liters per minute, wherein the device is adapted to aerosolize the active agent formulation and wherein the active agent formulation is (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant.

43. The device of claim 42 wherein the device is adapted to deliver an aerosolized insulin formulation to the lungs.

44. The device of claim 42 wherein the orifices are sized so that the aerosolized active agent formulation may be delivered at an inspiratory flow rate of 10 liters per minute or less.

45. The device of claim 42 wherein the active agent formulation is a powder and wherein the device is adapted to aerosolize the active agent formulation.

46. The device of claim 42 wherein the active agent formulation is contained in a blister and wherein the device is adapted to receive the blister.

47. A device for delivering an aerosolized active agent to the lungs of a human patient, said device comprising:

a chamber in flow communication with a mouthpiece;

means for aerosolizing the active agent; and

means for limiting an inspiratory flow rate through the mouthpiece to less than 17 liters per minute,

whereby an aerosolized active agent formulation in the chamber may be delivered to the human patient, the active agent formulation being (i) a powder, (ii) a solution, suspension, or slurry that may be nebulized, or (iii) suspended or dissolved in a propellant.

48. The device of claim 47 wherein the inspiratory flow rate is limited to 10 liters per minute or less.

49. The device of claim 47 wherein the device is adapted to deliver an aerosolized insulin formulation to the lungs.

50. The device of claim 47 further comprising means for aerosolizing the active agent.

51. The device of claim 47 wherein the active agent formulation is a powder and wherein the device is adapted to aerosolize the active agent formulation.

52. The device of claim 47 wherein the active agent formulation is contained in a blister and wherein the device is adapted to receive the blister.

(9) Evidence Appendix

none

(10) Related Proceedings Appendix

none